Perioperative Complications of Liver Resection in the Elderly With Hepatocellular Carcinoma: A Comparison With Younger Patients

Ruey-Horng Rau[1,2]*, Jei-Yu Huang[1], Chih-Lin Yang[1], Hsin-Jung Tsai[1], Chea-Ying Chen[1], Hsuan-Chih Lao[1], Chun-Jen Huang[1,2]

[1]Department of Anesthesia, Mackay Memorial Hospital, and [2]Mackay Medicine Nursing and Management College, Taipei, Taiwan.

SUMMARY

Background: Liver resection surgery in patients with hepatocellular carcinoma is a high-risk procedure with an in-hospital mortality rate around 5%. Patient age and volume of blood loss were found to be independent predictive factors of long-term outcomes in previous studies. We sought to clarify the age-related differences in the perioperative complications during the whole admission for liver resection surgery.

Methods: This retrospective study included 210 patients scheduled for elective liver resection from July 2006 to July 2008. The characteristics of the patients, intraoperative events, and postoperative complications were retrieved from medical charts, anesthesia records stored in a computer database, and the quality assurance system in our department. The patients were divided into two groups: Group A, aged 60 years or older ($n = 91$); and Group B, aged younger than 60 years ($n = 119$). Postoperative complications and intraoperative parameters were compared using the Student's t test for continuous data, and χ^2 test for categorical data. Correlations of age with blood loss, operation time, urine output, length of intensive care unit stay, total admission time, and intubation time were examined with the Pearson's correlation. Analysis of variance was used to investigate the endotracheal intubation time with different postoperative pain control methods.

Results: No differences in intraoperative blood loss, total operation time, urine output during surgery, in-hospital death, difficulty of operation, and incidence of massive blood loss and oliguria were found between the two groups. The length of intensive care unit stay and total admission time were significantly longer in the elderly group ($p = 0.04$ and 0.01, respectively). There was a higher incidence of postoperative respiratory complications in the elderly as revealed by a longer intubation time in Group A than in Group B ($p = 0.03$).

Conclusion: In contrast to some surgeries for emergency conditions such as long bone fracture or acute abdomen, the perioperative complications in the elderly receiving elective liver resection surgery did not differ markedly from those of younger patients. However, elderly patients would benefit even more if comprehensive postoperative care or newly improved therapies can be provided to lessen the incidence of perioperative respiratory complications. [International Journal of Gerontology 2009; 3(2): 101–107]

Key Words: general anesthesia, geriatrics, hepatocellular carcinoma, perioperative care, surgery

Introduction

Almost all elderly people have disabilities or disorders in more than one organ system when they present to hospital. Therefore, taking good care of these patients necessitates the cooperation of specialists from a variety of medical and paramedical fields. The elderly population is the most explicit target of so-called "total patient

*Correspondence to: Dr Ruey-Horng Rau, Department of Anesthesia, Mackay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail: johnson@ms1.mmh.org.tw
Accepted: March 13, 2009

care" and "patient-centered care", which are the mainstream of current medicine[1]. In the perioperative period, the concept of patient-centered care must be reemphasized, and good teamwork, which includes interns, surgeons, anesthetists, intensive care providers and other specialists, can assure elderly patients of their safety in and smooth recovery from major surgery.

There is a steady trend for the proportion of aging people to become greater in modern society, provided that the rapid progress of health care and improvement of the living environment continue. Hepatocellular carcinoma (HCC), one of the most common malignant tumors worldwide with a higher incidence in the elderly, is expected to become a real challenge for surgeons and anesthetists in performing surgical treatment, which can cause severe complications in elderly patients. Currently, there are many treatment options for patients with HCC, such as percutaneous ethanol injection therapy, microwave coagulation therapy, and percutaneous radiofrequency ablation. All these less invasive operations can be acceptable alternatives to hepatic resection in the elderly, but the best treatment for patients in this age group remains controversial[2].

Many chronic diseases, such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease and dementia, have a much higher prevalence in the elderly than in younger people, and the age-related complications resulting from these chronic diseases are expected to be more serious and lethal than in younger populations. In addition, aging itself can limit and restrict the functional reserves of cardiovascular, pulmonary, renal, endocrine and central nervous systems, which are all vital for a patient to tolerate and recover from a severe invasive intervention such as surgical resection in HCC.

Surgical resection of HCC is the only treatment choice for some patients and is a major operation with a considerable incidence of morbidity and mortality in all patient groups, especially in patients with liver cirrhosis or limited liver function[2]. The resection procedure is sometimes accompanied by massive blood loss in patients with a bleeding tendency or adhesions of internal organs resulting from prior surgery. This can lead to derangement of electrolytes and endocrine hormones, resulting from a malfunction of the renal system complicated by chronic liver disease, and fluctuations of blood pressure that can decrease the amount of blood perfusion to the liver. This results in poor prognosis for the immediate or long-term outcome of the patient.

In the meantime, the anesthetist must overcome the severely compromised lung function of an elderly patient undergoing such an upper abdominal surgical procedure to prevent pulmonary complications such as pneumonia or atelectasis, to minimize the possibility of the development of sepsis, which is considered a major cause of morbidity and mortality. Moderate to severe hypothermia, resulting from massive blood loss, and long operative times do not allow the patients, whose condition reduces the metabolism of anesthetic drugs, to recover muscle power and coagulation. A rapidly changing intravascular volume requires a fluid management strategy to provide the patient with stable cardiovascular function.

In this retrospective study, we determined the short-term incidence of morbidity and mortality of HCC patients selected for liver resection. We compared the differences in the complications in elderly and younger patient populations, and investigated whether a more effective pain control strategy could provide the patients with faster weaning from endotracheal intubation.

Materials and Methods

The local ethics committee approved this study. Between July 2006 and July 2008, 210 HCC patients were sent to our operation rooms for liver resection surgery. We included these patients in this retrospective study by searching the medical information system designed and maintained in our anesthesia department. Variables related to the patients' past medical history and intraoperative complications were obtained from electronic anesthesia records stored in a computer database. When information from the anesthesia records was not detailed, we searched the paper medical records as an alternative resource. Variables related to postoperative anesthesia-related complications of these patients were collected from our quality assurance system, while variables related to other complications also came from the paper medical records.

The factors related to perioperative complications were: (1) massive blood loss, if the patients had more than 1,000 mL of blood loss during the operation; (2) prolonged intubation, if the patients could not be weaned from intubation within 24 hours for any reason; (3) oliguria, if the urine output during the whole operation was less than 300 mL despite aggressive diuretic treatments and fluid replacement; (4) prolonged

intensive care unit (ICU) stay, if patients stayed in the ICU for more than 3 days for any reason; (5) prolonged admission, if patients could not be discharged without any complication and stayed in hospital for more than 17 days for any reason; and (6) prolonged surgery, if the whole operation could not be carried out within 3 hours for any reason.

To find any difference in the incidence of perioperative complications between elderly patients and younger patients, the 219 participants were divided into two separate groups: Group A, which included patients aged 60 years or older; and Group B, which included patients younger than 60 years.

Statistical Analysis

All scaled data are expressed as mean ± standard deviation. The blood loss, age, operation time, urine output, length of ICU stay, total admission time, and intubation time were compared between Group A and Group B using the unpaired Student's *t* test (two-tailed) and Levene's test for equality of variances. The incidence of massive blood loss, prolonged intubation, oliguria, prolonged ICU stay, prolonged admission, and operation difficulty were compared using the nonparametric χ^2 test (two-tailed). Comparisons according to age were determined for the following variables: blood loss, operation time, urine output, length of ICU stay, total admission time, and intubation time. Analysis of variance with *post hoc* Tukey test was examined for endotracheal intubation duration with pain control methods as factors. All statistical analyses were performed using SPSS version 16.0.1 (SPSS Inc., Chicago, IL, USA) for Windows. A $p < 0.05$ was considered statistically significant.

Results

For all 210 patients, the mean age was 58.3 ± 13.6 years (range, 11–86 years). When divided into the two groups with a cut-off of 60 years, the mean age of the older group was about 20 years older (70.2 ± 5.9 years) than the younger group (49.0 ± 10.2 years). The operation time, blood loss, and urine output of the two groups were almost identical, with no significant differences (Table 1). However, the length of ICU stay, total admission time, and intubation time of the two groups showed statistically significant differences (Table 1). These outcomes implied that the elderly patients did not have more intense surgical techniques than the younger patients, but the elderly patients did need much more intensive care postoperatively to recover from the severe surgical trauma.

Our patients had an overall 4.76% incidence of in-hospital death, with a higher incidence in the elderly group ($n = 7$, 7.6%) than in the younger group ($n = 3$, 2.5%), although the difference was not statistically significant ($p = 0.08$). The surgical operation of liver resection is a time-consuming procedure, and lasted for more than 3 hours in 61.5% of elderly patients and in 66.6% of younger patients. Massive blood loss is also a common complication in liver resection surgery, and 41.8% of elderly patients and 33.6% of younger patients suffered from this. The incidence of oliguria was less common than blood loss, but there were still 20.9% of elderly patients and 26.1% of younger patients whose renal function was compromised intraoperatively. The incidences of postoperative complications were especially prominent in elderly patients. The incidence of prolonged ICU stay, prolonged admission, and prolonged intubation were 26.4%, 47.3% and 24.2%, respectively, in the elderly, which were significantly more than in younger patients, with 9.2%, 20.2% and 9.2%, respectively (Table 2). Although the incidences of postoperative complications were much higher in the elderly patients, aging alone could not account for this. The correlations of age with blood loss, operation time, urine output, length of ICU stay, and intubation time were weak (Table 3); only the correlation of age with total admission time was statistically significant ($p = 0.01$). This information suggests that age is not an independent risk factor for many postoperative complications, and other confounders such as the underlying diseases of the patients should be examined for these morbidities. The pain control methods did not affect the endotracheal intubation time ($p = 0.075$), and the patients with epidural analgesia were not weaned off the intubation more quickly than other patients (Table 4). Another study with a larger case number may remove the uncertainty resulting from the statistical type II error.

Discussion

Mortality associated with anesthesia and surgery is defined as the death rate within 30 days of operation. Advances in anesthetic/surgical techniques and perioperative care have substantially reduced surgery-related mortality[3]. However, the overall mortality in

Table 1. *Patients' baseline demographic characteristics and conditions during the surgical operation and admission period**

	Group A (≥60 yr; $n=91$)	Group B (<60 yr; $n=119$)	p
Age (yr)	70.2±5.9	49.0±10.2	<0.01†
Operation time (min)	220.2±75.3	219.7±93.8	0.962
Blood loss (mL)	1,226.9±1,591.7	1,269.9±1,867.4	0.861
Urine output (mL)	599.4±388.5	683.4±590.2	0.216
ICU stay (d)	4.3±9.2	2.3±5.1	0.048†
Total admission time (d)	20.5±15.1	14.6±9.7	0.01†
Intubation time (hr)	30.8±109.2	7.73±32.2	0.034†

**Data are presented as mean±standard deviation; †statistically significant at $p<0.05$ (two-tailed). ICU=intensive care unit.*

Table 2. *The incidence of perioperative complications in the elderly group (Group A) and the younger group (Group B)**

	Group A (≥60 yr; $n=91$)	Group B (<60 yr; $n=119$)	p
Death (in hospital)†	7 (7.7)	3 (2.5)	0.08
Difficult operation‡	56 (61.5)	78 (65.5)	0.55
Massive blood loss§	38 (41.8)	40 (33.6)	0.23
Oliguria‖	19 (20.9)	31 (26.1)	0.38
Prolonged ICU stay¶	24 (26.4)	11 (9.2)	0.01**
Prolonged admission††	43 (47.3)	24 (20.2)	<0.01**
Prolonged intubation‡‡	22 (24.2)	11 (9.2)	0.03**

**Data are presented as n (%); †if the patient died in hospital after operation directly or indirectly as a result of surgery; ‡if the whole surgical procedure lasted for more than 3 hours; §if blood loss was above 1,000 mL during the whole surgical procedure; ‖if the patient's intraoperative urine output was under 300 mL; ¶if the patient stayed in the ICU for more than 3 days for any reason; **statistically significant at $p<0.05$ (two-tailed); ††if the patient could not leave hospital in the operation course for more than 17 days; ‡‡if the patient could not be weaned off endotracheal intubation in 24 hours. ICU=intensive care unit.*

Table 3. *Correlation of patients' age with blood loss, operation time, urine output, intensive care unit (ICU) stay, total admission time, and intubation time*

	Pearson's correlation	p
Blood loss	–0.05	0.48
Operation time	0.006	0.93
Urine output	–0.46	0.51
ICU stay	0.077	0.27
Total admission time	0.178	0.01*
Intubation time	0.081	0.25

**Statistically significant at $p<0.05$ (two-tailed).*

all cases remains at 1.2%, rising to 2.2% in patients aged 60–69 years, 2.9% in those aged 70–79 years, 5.8–6.2% in patients aged 80–89 years, and 8.4% in those aged older than 89 years[4]. Major surgery further increases elderly mortality; for example, emergency abdominal surgery results in a 9.7% mortality for patients over 80 years of age, thoracotomy in a 17% mortality for those over 70 years of age, and any major surgical procedure in a 19.8% mortality for those over 90 years of age[5,6]. In our hospital, the mean age of the patients who were diagnosed with HCC and received liver resections in the past 2 years was 58.3±13.6 years, several years younger than those in Japan (63.9 years in men and 67.3 years in women)[7], a country with the same high prevalence of HCC as Taiwan.

The major side effect accompanying liver resection is blood loss. Although the volume of blood loss fluctuated case by case, as revealed by a large ratio of standard deviation to mean value in the intraoperative blood loss volume of elderly and younger patients (1,226.9±1,591.7 mL and 1,269.9±1,867.4 mL, respectively), there were still 41.8% of elderly patients and 33.6% of younger patients whose blood loss volume exceeded 1,000 mL. The well-known complications of massive blood volume transfusion consist of thrombocytopenia, coagulation factor depletion, oxygen affinity changes, hypocalcemia, hyperkalemia, acid–base disturbance, hypothermia, and the rare, but possibly fatal, complication of acute respiratory distress syndrome.

Table 4. *Analysis of variance of endotracheal intubation time with pain control methods as a factor (post hoc Tukey test)*

(I) pain	(J) pain	Mean difference (I – J)	Standard error	Significance	95% confidence interval	
					Lower bound	Upper bound
0	1	3.452	16.745	0.977	–36.08	42.99
	2	26.787	16.724	0.247	–12.70	66.27
1	0	–3.452	16.745	0.977	–42.99	36.08
	2	23.336	11.228	0.097	–3.18	49.85
2	0	–26.787	16.724	0.247	–66.27	12.70
	1	–23.336	11.228	0.097	–49.85	3.18

0 = patients with pain control of conventional intramuscular opioids injection (n = 30); 1 = patients with self-controlled intravenous opioid infusion devices (n = 90); 2 = patients with self-controlled epidural opioid infusion devices (n = 90).

Some of these complications, such as thrombocytopenia, coagulation factor depletion, hypocalcemia and hypothermia, if not treated promptly and appropriately in the elderly, can eventually lead to a vicious cycle of bleeding. Because of the many physiologic changes in aging, hypothermia after massive blood transfusion is expected to occur more often in the elderly than in the younger population. Hypothermia can, furthermore, complicate the pharmacodynamics and pharmacokinetics of anesthetics, sedative drugs and other adjuncts used perioperatively, and can certainly contribute to the prolonged endotracheal intubation time in the elderly. These findings in our study are compatible with the research by Chok et al[8] in that massive intraoperative blood loss is related to a significantly higher complication rate and affects the long-term outcome in patients having curative liver resection for HCC. The low central venous pressure technique, which is achieved by fluid restriction or infusion of vasodilatory drugs intraoperatively, is believed to be a useful technique for reducing the volume of blood loss in liver resection and transplantation surgeries[9]. In the elderly population, considering the limited cardiovascular reserve and the possibility of degeneration of the autoregulatory function of most vital organs, extensive applications of this technique in geriatric patients should only be done after a thorough preoperative evaluation of the patients.

With limited functional reserve, an acute large blood loss can promptly insult the vital organs in elderly patients because of insufficient perfusion to these vulnerable organs. The studies of blood volume in geriatric populations can be traced back to 1959; they showed that normal geriatric populations consistently have a low mean value and a wide range. Another important fact was that in young patients, there was a definite correlation of red blood cell volume and total body water with body weight, whereas in elderly patients, there was no correlation[10]. These two special characteristics render the geriatric populations into a critical situation in which if an acute blood loss occurs during a liver resection surgery, a judgment must be made promptly by the attending anesthetists to replace the blood loss appropriately; severe hypotension or acute pulmonary edema can ensue from the rapid overexpansion of intravascular volume. Dysfunction of the autonomic nervous system is another concern in the elderly. The two most significant deteriorations in the autonomic system on aging are a decrease in response to beta-receptor stimulation and, thus, a feedback increase in the catecholamine levels arising from sympathetic nervous system activity[11]. Normally, beta-receptor-mediated mechanisms act to increase the heart rate, venous return and systolic arterial pressure, while preserving preload reserve. In contrast, the attenuated beta-receptor response in the elderly during stress, such as during surgery, is associated with a decreased maximal heart rate and decreased peak ejection fraction. Many anesthetics, including inhalation agents and narcotics, also severely desensitize the heart to stimulation by a beta-receptor agonist. Therefore, when rapid blood replacement is needed to reestablish the normal intravascular blood volume, the speed of infusion of the fresh blood or crystalloid fluid should be monitored according to the heart rate to prevent overstretching of the aged heart. As far as insensitivity of the elderly to catecholamines is concerned, the attending anesthetists must select a potent inotropic agent as the first drug of choice to resuscitate the compromised cardiovascular system in such a critical operation as liver resection in the elderly. Diastolic dysfunction of the left ventricle, which mainly arises from left ventricular hypertrophy on aging, is also a complication. Diastolic dysfunction

or failure is often related to systemic blood pressure and does not necessarily suggest volume overload, which is a common complication in patients experiencing rapid intravascular volume expansion for massive blood loss. Differentially diagnosing diastolic or systolic dysfunction is hard, because both functional defects present the same clinical picture. Making the correct diagnosis is imperative for the patient in that interventions commonly used in systolic failure, such as diuretics and inotropes, may worsen diastolic dysfunction in the elderly. An intraoperative transesophageal echocardiogram, with the probe in the middle portion of the esophagus, can show a clear cross-sectional view of the middle portion of the left ventricle. It can thus provide important information on both preload volume and contractility of the left ventricular myocardium, but the possibility of bleeding, which may be a complication during insertion of the probe into the esophagus in an HCC patient, should be carefully considered[12].

Preoperative and postoperative management of pulmonary problems is of particular importance. In general, in surgical patients 65 years and older, the incidence of common postoperative morbidities is 17% for atelectasis, 12% for acute bronchitis, 10% for pneumonia, 6% for heart failure or myocardial infarction (or both), 7% for delirium, and 1% for new focal neurologic signs[13]. In our study, the endotracheal intubation duration was significantly different in the elderly and younger age groups (30.8 ± 109.2 hours vs. 7.73 ± 32.2 hours; $p = 0.034$), and complications of the respiratory system may be more prominent than those of the cardiovascular system in the perioperative period of liver resection. These complications may partially arise from the lung structure changing with age, including the loss of elastic recoil after reorganization of collagen and elastin in the lung parenchyma, altered surfactant production, enlargement of the respiratory bronchioles and alveolar ducts, a tendency for early collapse of the small airway on exhalation, and the increased size of the interalveolar pores of Kohn. All these age-related functional changes lead to an increased closing capacity, decreased diffusing capacity, and increased anatomic dead space in the elderly population.

Although aging itself can make the elderly vulnerable to perioperative respiratory compromise, anesthetics and the procedure of liver resection can worsen the limited functional reserve of the lungs in elderly patients. In 1976, Gamsu et al.[14] compared the rate of tantalum clearance from the lungs of postoperative patients who had received general anesthesia for intra-abdominal or lower extremity operations. In patients receiving general anesthesia for intra-abdominal surgery, the retention of tantalum was demonstrated for as long as 6 days, severely prolonged when compared with patients with lower extremity surgery[14]. The degree of impairment of the clearance of sputum in the tracheobronchial tree is also proportional to the administration time of endotracheal-intubated anesthesia with positive ventilation. According to the above studies, the long operative time of liver resection surgery may make the elderly patients prone to sputum lodging in the already-obstructed tracheobronchial tree. In addition to aggressive suction of the pulmonary secretions through the endotracheal tube intraoperatively, the attending anesthetists should use warmed, humidified gas and choose an inhaled anesthetic, such as sevoflurane, with a weaker direct cilioinhibitory effect than other agents, to maintain the respiratory function of the elderly as much as possible[15]. Other anesthesia adjuncts such as benzodiazepines, opioids and sedative drugs may also produce an exaggerated respiratory depressant effect in the elderly, whose ventilatory responses to hypoxia, hypercapnia and mechanical stress are impaired secondary to reduced central nervous system activity[16]. The attending anesthetist should prescribe these agents in a titration-to-effect method and reduce the drug dosage as needed.

How upper abdominal surgeries compromise respiratory function has been studied in patients and animal models. The changes in the pattern of breathing after upper abdominal surgeries were similar to those changes described in patients with bilateral paralysis of the diaphragm or severe generalized neuromuscular disease with impaired diaphragm function, or in dogs after complete diaphragmatic paralysis[17]. The mechanisms of the decreased diaphragm activity after upper abdominal surgery are unknown. Many researchers have proposed abdominal pain as a mechanism for the reduced functional residual capacity after upper abdominal surgery; but in another animal model, local irritation, inflammation and trauma secondary to upper abdominal surgery were proposed by authors to be the underlying cause which may lead to local mechanical failure of the diaphragm[18]. In this study, patients receiving epidural analgesic infusion, which was regarded as a more effective pain control method than that of intravenous opioid injection, were not weaned off endotracheal intubation more quickly than other

patients. This finding may suggest that postoperative pain is not the only dominating factor that affects the endotracheal intubation time; on the other hand, age-related decreased lung function reserve and other underlying diseases should be independent risk factors for prolonged endotracheal intubation.

Elderly people have been largely excluded from high-quality trials, and much of the evidence comes from a case series of selected patients, which demonstrate what is possible. However, major elective operations, which include cardiac, vascular, oncologic and orthopedic surgeries, can be performed on patients over 75 years of age with good outcomes and adverse event rates similar to those of younger patients[19]. Our study confirmed that in comparing the elderly and younger population, there was no statistically significant difference in certain perioperative parameters, including intraoperative blood loss, urine output, duration of operation, difficulty of operation, in-hospital death rate, incidence of massive blood loss, and incidence of oliguria. However, respiratory function complication in the elderly population was significantly different to that of the younger population. Further studies should focus on strategies to minimize morbidities and mortalities resulting from perioperative respiratory complications in the elderly.

In conclusion, although liver resection for HCC carries some inevitable complications such as massive intraoperative blood loss, the elderly prove to be appropriate candidates for this high-risk surgery. This is providing that the preoperative evaluation of all vital organs' functional reserve are thoroughly examined, intraoperative blood losses are carefully replaced, fluctuations of blood pressure are managed, and postoperative respiratory complications are minimized as much as possible by means of aggressive pain control, chest care, inhalation therapy, and other suitable maneuvers. There are still some uncertainties that may result from the type II statistical error in this study; a further prospective study with greater sample size may resolve these.

References

1. Shih SC. Update and integration of knowledge of gerontology. Int J Gerontol 2008; 2: 143–4.
2. Kaibori M, Matsui K, Ishizaki M, Saito T, Kitade H, Matsui Y, et al. Hepatic resection for hepatocellular carcinoma in the elderly. J Surg Oncol 2009; 99: 154–60.
3. Jin F, Chung F. Minimizing perioperative adverse events in the elderly. Br J Anaesth 2001; 87: 608–24.
4. Pedersen T, Eliasen K, Henriksen E. A prospective study of mortality associated with anaesthesia and surgery: risk indicators of mortality in hospital. Acta Anaesthesiol Scand 1990; 34: 176–82.
5. Kettunen J, Paajanen H, Kostiainen S. Emergency abdominal surgery in the elderly. Hepatogastroenterology 1995; 42: 106–8.
6. Ackermann RJ, Vogel RL, Johnson LA, Ashley DW, Solis MM. Surgery in nonagenarians: morbidity, mortality, and functional outcome. J Fam Pract 1995; 40: 129–35.
7. Ikai I, Itai Y, Okita K, Omata M, Kojiro M, Kobayashi K, et al. Report of the 15th follow-up survey of primary liver cancer. Hepatol Res 2004; 28: 21–9.
8. Chok KS, Ng KK, Poon RT, Lo CM, Fan ST. Impact of postoperative complications on long-term outcome of curative resection for hepatocellular carcinoma. Br J Surg 2009; 96: 81–7.
9. Massicotte L, Lenis S, Thibeault L, Sassine MP, Seal RF, Roy A. Effect of low central venous pressure and phlebotomy on blood product transfusion requirements during liver transplantations. Liver Transpl 2006; 12: 117–23.
10. Waltemath CL, Harkness TT. Blood volume studies on normal geriatric subjects. Anesth Analg 1963; 42: 551–8.
11. Rooke GA. Autonomic and cardiovascular function in the geriatric patient. Anesthesiol Clin North America 2000; 18: 31–46, v–vi.
12. Tresch DD. Clinical manifestations, diagnostic assessment, and etiology of heart failure in elderly patients. Clin Geriatr Med 2000; 16: 445–56.
13. Seymour DG, Vaz FG. A prospective study of elderly general surgical patients: II. Post-operative complications. Age Ageing 1989; 18: 316–26.
14. Gamsu G, Singer MM, Vincent HH, Berry S, Nadel JA. Postoperative impairment of mucous transport in the lung. Am Rev Respir Dis 1976; 114: 673–9.
15. Matsuura S, Shirakami G, Iida H, Tanimoto K, Fukuda K. The effect of sevoflurane on ciliary motility in rat cultured tracheal epithelial cells: a comparison with isoflurane and halothane. Anesth Analg 2006; 102: 1703–8.
16. Zaugg M, Lucchinetti E. Respiratory function in the elderly. Anesthesiol Clin North America 2000; 18: 47–58, vi.
17. Ford GT, Whitelaw WA, Rosenal TW, Cruse PJ, Guenter CA. Diaphragm function after upper abdominal surgery in humans. Am Rev Respir Dis 1983; 127: 431–6.
18. Road JD, Burgess KR, Whitelaw WA, Ford GT. Diaphragm function and respiratory response after upper abdominal surgery in dogs. J Appl Physiol 1984; 57: 576–82.
19. Preston SD, Southall AR, Nel M, Das SK. Geriatric surgery is about disease, not age. J R Soc Med 2008; 101: 409–15.